REMARKS

This Amendment is being filed in response to the Office Action dated June 16, 2010.

Claims 77 and 94 have been amended to eliminate the optional step of removing non-aqueous solvent from the suspension.

Newly presented Claims 107-111 have been added. No new matter is added by the present claims. Support can be found in claims 1-76 as originally filed, page 5, line 22 to page 9, line 5 of the specification as originally filed[1] and Examples 1 and 4 of specification as originally filed[2].

Upon entry of the present Amendment, claims 77-80, 82-98 and 107-111 will be pending in the application.

On pages 3-8 of the Office Action the Examiner rejected claims 77-80 and 82-98 under 35 U.S.C. § 103(a) as being unpatentable over United States Patent No. 6,187,765 (hereinafter "Harris").

Reconsideration is requested.

As acknowledged by the Examiner, Harris does not teach a method wherein the steroid remains in suspension after the solvent is removed (*see* June 16, 2010 Office Action at page 5, lines 3-4). However, the Examiner alleges that the additional steps of removing the solvent by filtration and drying as taught by Harris are not excluded by Applicant's claim language because the term "comprising" is interpreted as broad and open. Furthermore, the Examiner alleges that these steps are not essential as there is no material effect on the end product.

Applicants respectfully disagree.

Claims 77 and 94 as herein amended no longer comprise a solvent removal step. In new claims 107 and 108 the solvent removal step is no longer optional - all or part of the non-aqueous solvent is removed to yield a sterile aqueous suspension having reduced non-aqueous solvent content. The sterile aqueous suspension having reduced non-aqueous solvent content is then treated to obtain a sterile aqueous suspension with a particle size distribution having a mass median diameter less than 10 μm.

Thus, the claimed methods do not include any drying step. The solvent removal step recited within claims 107 and 108 merely removes non-aqueous solvent from an aqueous

[1] *See* Paragraphs 0023-0041of United States Published Application 2005/0222108.
[2] See Paragraphs 0044-0047 (Example 1) and Paragraphs 0059-0080 (Example 4) of United States Published Application No. 2005/0222108.

suspension so that at the end of the solvent removal step the steroid particles are suspended in an aqueous suspension having reduced non-aqueous solvent content.

Furthermore, since each step of the method utilizes the solution or suspension obtained in a preceding step, it is apparent that Applicant's claimed method does not comprise an intermediate drying step.

Example 1 of Harris produces sterile mometasone furoate monohydrate *per se* by a process that finishes with a drying step, to produce a dry product (step 10 of example 1). This dry product is then used to formulate various pharmaceutical compositions, each having different concentrations of active and excipients (see examples 2, 3, 5 and 6). Thus, a person of skill in the art would understand that Harris considered it essential to produce a sterile dry product as this enables the easy formulation of any number of desired compositions.

Further, Harris teaches that "[i]t is preferred to produce the mometasone furoate monohydrate under sterile conditions, conduct the drug micronization in a sterile environment, and perform a sterile packaging operation". This, read in combination with examples 1, 2, 3, 5 and 6, provides additional direction that the processes of Harris are separate and distinct parts of a two stage method.

Thus, the essential first stage of the method of Harris is to produce dry sterile mometasone furoate monohydrate. Conversely, Applicant's claimed invention provides a single stage method for preparing a sterile pharmaceutical composition of a steroid. In *In re Freed*, 425 F.2d 785 (CCPA 1970), the claimed invention was a single stage process for producing calcium pantothenate whereas the prior art disclosed a two stage reaction. The court held that the single stage process was not obvious over the two stage process disclosed in the prior art. The court explained that:

> it seems logical and reasonable to infer that one teaching a chemical reaction process would set out the least number of reactions thought necessary to accomplish the desired objective.

Freed, 425 F.2d at 788.

Thus, following the clear teaching of Harris that a two stage method is essential, a single stage method would not be obvious to the skilled person.

Furthermore, it would not be obvious for a person of skill in the art to first seek to combine the processes of examples 1 and 2 of Harris and then to omit the drying step of example 1. The suspension of example 1 (last present in step 8) comprises sterile mometasone furoate monohydrate in suspension with water and acetone. Example 2 begins by preparing a sterile excipient solution of polysorbate 80, citric acid monohydrate, sodium

citrate dehydrate and sodium chloride, to which a precise number of grams of dry mometasone furoate monohydrate are added. Thus, if the mometasone furoate monohydrate were still in suspension there would be a number of problems, including: (i) the presence of acetone in the suspension, whereas this would previously have been removed by drying; and (ii) the mometasone furoate monohydrate would be in a dilute suspension comprising a large amount of water, making it difficult to calculate the precise amount of mometasone furoate monohydrate present or indeed to remove a precise amount of mometasone furoate monohydrate from the suspension. This dilute suspension could not simply be added to the excipients prepared in steps 1 and 2 of example 2 without a significant number of calculations and alterations to the process of example 2.

Thus, to convert the two stage method of Harris into the single stage method of Applicant's invention would require the skilled person to make a significant number of complex changes to the processes of examples 1 and 2 of Harris.

The skilled person reading Harris would understand that the two stage method is essential and moreover, even if they were seeking a simpler method, it would not be obvious to make significant amendments to both parts of the Harris method in order to combine the separate processes. It would be far easier to follow the Harris method exactly as set out, producing dry sterile mometasone furoate monohydrate and mixing this with excipients as desired.

In summary, the method of the present invention does not merely amount to a reversal of the steps of the method disclosed in Harris. Rather, the claimed invention recites a single stage process that is not obvious from the teachings of Harris.

Based upon the foregoing amendments and representations, Applicants respectfully submit the rejections of the claims in the above-identified application have been overcome and should be withdrawn. Early and favorable action is earnestly solicited. If the Examiner does not believe the pending claims are in the form for allowance, Applicants invite the Examiner to call the undersigned to discuss ways to further expedite prosecution of this application.

Applicants have previously paid for thirty claims, including three independent claims. After entry of the present Amendment the application will contain twenty six total claims, and four independent claims. Submitted herewith is the fee for one additional independent claim. If there are any additional fees or overpayments please charge them to deposit account number 505222.

An early and favorable action is earnestly solicited.

Respectfully submitted,

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